Aortic regurgitation imposes a volume overload on the left ventricle. Adaptation to this load occurs by an increase in chamber size such that the total stroke volume increases in proportion to the regurgitant volume while the forward stroke volume and cardiac output remain normal. In spite of left ventricular enlargement, the wall stress can remain normal due to myocardial hypertrophy and to geometric alterations by which the ventricle assumes a more spherical shape.[8,9] Myocardial function is usually well preserved until the late stages of chronic aortic regurgitation.

The left ventricle responds to a volume overload initially by near-maximal use of the Frank-Starling mechanism. The ability to increase the total stroke volume by this mechanism alone, however, is limited. Ultrastructural studies of acutely overdistended canine left ventricles show that the midwall sarcomere lengths average $2.25\mu$, a magnitude which is near the apex of the sarcomere length-tension curve.[15] Further distention of the sarcomere down the descending limb of the Frank-Starling curve is resisted even at very high filling pressures. This maximal use of "preload reserve" in the acute volume-distended ventricle is not associated with a significant change in mean Vcf or other ejection phase indices.[16] Therefore, the left ventricle appears to adapt more readily to acute volume rather than to acute pressure overload.

As the volume overload persists, the left ventricular end-diastolic volume progressively increases. This increase in volume requires adaptations other than the Frank-Starling phenomenon. Again, ultrastructural studies from chronically volume overload dog hearts have shown that midwall sarcomere lengths averaged $2.19\mu$, not significantly different from acutely distended dog hearts.[17] Consequently, the major adaptation of the left ventricle to chronic volume overload involves the addition of new sarcomeres in series, allowing the ventricle to increase its end-diastolic volume dramatically without an accompanying change in end-diastolic pressure. The ejection phase indices (normalized per unit length) generally remain normal even with greatly dilated hearts.[18] For example, in dogs with volume overloads induced by a large aortocaval fistula, the maximum velocity of shortening (V max) measured from the force-velocity curve remained normal even when pronounced peripheral edema, ascites and pleural effusion developed in these dogs.[19] However, it is well known that in humans with chronic aortic regurgitation, myocardial function eventually and insidiously deteriorates. The structural or biochemical changes that lead to irreversible depression of the contractile state in chronic volume overloading remain unknown.

It is to be hoped that further laboratory investigation will define these changes and allow their earlier clinical detection[20] so that earlier surgical intervention can prevent irreversible damage.

DR. JOHNSON: *As Drs. Tsuji and Peterson have discussed, the pathophysiology and adaptations to the increased pressure burden imposed by aortic stenosis, and the volume overload associated with aortic regurgitation, are distinctly different, and are responsible for different natural histories and different clinical presentations in these two disorders. Dr. Robert Engler will now discuss the clinical features of aortic valve disease in the context of our knowledge of the pathophysiology of aortic valve disease.*

## Historical and Physical Findings in Patients with Aortic Valve Disease

ROBERT L. ENGLER, MD*

PATIENTS WITH AORTIC STENOSIS commonly come to medical attention because of the detection of a heart murmur in the absence of associated symptoms, or they may present with one or more of the classical symptoms associated with aortic stenosis: congestive heart failure, ischemic chest pain, or syncopal/semisyncopal episodes.[21] In a patient with suspected hemodynamically significant aortic stenosis, meticulous attention should be paid to the details of each of these symptom complexes.

Initial presentation with congestive heart failure is uncommon in a patient with aortic stenosis who has neither a history of heart murmur nor previous symptoms. Usually a history of insidious and rather subtle progression of fatigue and dyspnea for the preceding months or years will be elicited, associated with gradual curtailment of activities almost unnoticed by the patient. However, a patient may suddenly develop symptoms of con-

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gestive failure if an added hemodynamic burden or insult occurs—loss of sinus rhythm, thyrotoxicosis, anemia, ischemia secondary to coronary artery disease, febrile state or the like. In the absence of these precipitating causes, signs and symptoms of overt congestive heart failure usually indicate that the patient is in the very late stages of the natural history of aortic stenosis and probably significant myocardial disease has developed.

The second major symptom associated with aortic stenosis is angina pectoris. In a significant proportion of cases, angina pectoris occurs in the absence of coronary artery disease and is secondary to the increase in myocardial oxygen demands imposed by increased left ventricular mass, associated with probable changes in subendocardial blood supply occurring in the setting of increased wall thickness, increased end-diastolic pressure and increased wall tension.[22] However, many patients with aortic stenosis, particularly those beyond the fifth decade, have angina pectoris in association with significant arteriosclerotic coronary artery disease.[23] In these patients it may be quite difficult to determine which is the dominant factor responsible for angina pectoris, and cardiac catheterization and coronary angiography may be indicated.

The third dominant symptom in aortic stenosis is that of syncope or presyncopal episodes. Syncope due to aortic stenosis is usually exertional or postexertional. Current evidence suggests that the mechanism of syncope in aortic stenosis is a lack of appropriate reflex vasoconstriction in nonexercising muscles[24] or in some patients acute left ventricular failure,[25] both of which may result in hypotension. This reflex activity may be due to inappropriate left ventricular baroreceptor responses to elevated left ventricular systolic pressure despite peripheral hypotension. Syncopal episodes are uncommon in the absence of either angina or some degree of congestive heart failure;[4] therefore, when an occasional patient presents with syncope as an isolated symptom in the setting of suspected significant aortic stenosis, the various cardiac and noncardiac causes for syncope must be diligently explored. Syncope may be caused by intermittent heart block due to extension of calcium from the aortic valves to the region of the atrioventricular junction in the adjacent interventricular septum, or by tachyarrhythmias, particularly those associated with the loss of atrial systole. If no other cause of syncope can be determined, the physician is obligated to seek supportive evidence that significant aortic valvular obstruction exists.

On physical examination in patients with aortic stenosis, a narrow peripheral arterial pulse pressure and a slow rising carotid pulse commonly are noted, but it should be kept in mind that the pulse pressure and pulse contour can be modified by arteriosclerosis, hypertension, or associated aortic regurgitation. For this reason, one gains the most information with respect to pulse volume and pulse contour by examination of the carotid pulse, which is least influenced by these factors. The jugular venous pulse may have a prominent A-wave due to hypertrophy of the interventricular septum, or may be normal unless right heart failure accompanies the late stages of aortic stenosis. On examination of the precordium in the typical case, an apical impulse is found that is not displaced but is sustained and diffuse, and usually there is a palpable presytolic impulse. If the cardiac apex is displaced, coexistent left ventricular myocardial disease, associated aortic regurgitation, or mitral regurgitation should be suspected. While a systolic thrill may be felt either at the apex or the base, particularly with the patient standing or sitting with the breath held in exhalation, the presence of a thrill does not necessarily imply severe valvular aortic stenosis and can be felt in patients with trivial aortic stenosis who have either a thin chest wall or a large stroke volume.[26] The important feature of the auscultatory examination is the character of the systolic ejection murmur, which in significant aortic stenosis persists through most of systole and peaks in the latter half of systole (Figure 4). If the aortic valve is rigid and immobile, the aortic second sound may be absent. With the prolongation of left ventricular ejection in aortic stenosis, there may be paradoxical splitting of the second heart sound. Commonly, an ejection sound accompanies aortic stenosis secondary to a mobile but congenitally abnormal valve; however, this finding is not a reliable indicator of the degree of obstruction. The presence of a fourth heart sound ($S_4$) in patients under age 40 implies significant aortic stenosis. The absence of a fourth heart sound in patients over the age of 40 would suggest that aortic stenosis and left ventricular hypertrophy are not severe; however, 15 percent of patients with critical aortic stenosis may lack an $S_4$.[27,28] An $S_3$ gallop, particularly in older patients, is very suggestive of associated myocardial disease or congestive heart failure.

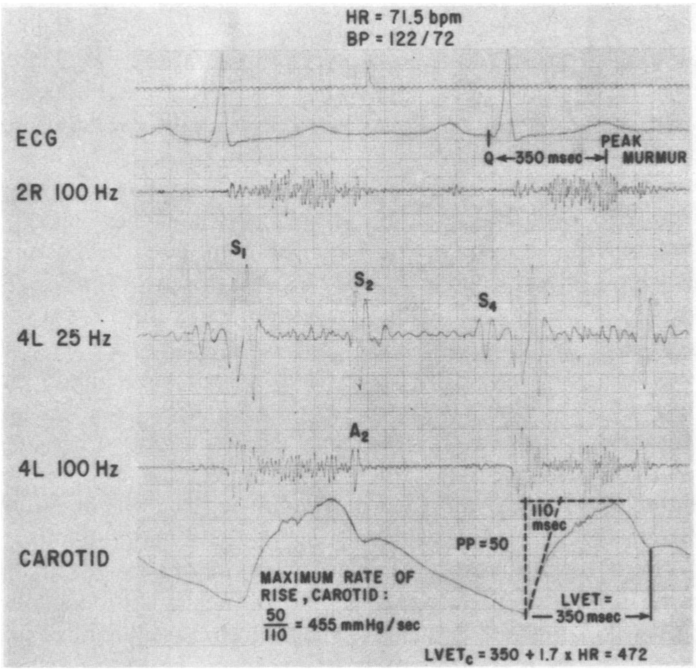


**Figure 4.**—Electrocardiogram (ECG), phonocardiogram and carotid pulse tracing from a patient with aortic stenosis. LVET=left ventricular ejection time; LVETc=rate and sex corrected LVET. PP=pulse pressure obtained with a sphygmomanometer, in this case 122−72=50 mmHg; A2=aortic closure sound; S1=first heart sound; S4=atrial diastolic gallop; 2R=second right intercostal space; 4L=fourth left intercostal space; HR=heart rate. BP=blood pressure.

Carotid upstroke time from onset of systolic rise in carotid pulse to peak **(horizontal dashed line)** is 250 msec, normal <120 msec.

The peak of the systolic murmur recorded at the second right interspace (2R) is 350 msec after the Q wave of the ECG; a murmur peaking more than 250 msec after the Q wave suggests significant aortic stenosis.

Examination of an elderly patient who is suspected of having aortic stenosis can be quite challenging. The expected slow upstroke of the carotid pulse and small pulse pressure present in significant aortic stenosis may be normalized by an arteriosclerotic peripheral arterial tree or by hypertension. Left ventricular hypertrophy, usually appreciated by palpation of the cardiac apex, may be masked by emphysema or an increased anteroposterior chest diameter. Likewise, the systolic murmur may be faint and best heard at the cardiac apex due to changes in the chest wall configuration accompanying age.[2] Therefore, one must pay careful attention to all of the features of the cardiac examination, and maintain a high index of suspicion that significant aortic stenosis exists. With such a patient, one commonly must proceed to noninvasive and occasionally invasive diagnostic studies to determine the presence or absence of significant aortic stenosis.

Another important and not uncommon clinical situation is a patient who initially presents with severe congestive heart failure and low cardiac output; in such a case, one might find a very unimpressive murmur in the setting of severe aortic stenosis. In *any* patient with congestive heart failure, a systolic murmur deserves careful examination and periodic reevaluation after therapy to assess whether or not treatment of the congestive heart failure has resulted in an improvement in cardiac performance and more reliable physical findings.

In chronic aortic regurgitation, left ventricular dilatation and changes in left ventricular mass and shape frequently maintain cardiac output and left ventricular function so that patients remain asymptomatic despite significant quantities of regurgitation. Mild dyspnea on exertion, fatigue and excessive sweating may be symptoms of moderate or severe disease. Angina pectoris tends to occur late in the course and may be "atypical" (it is more frequent at night, while patients are supine).[29]

In patients with acute severe aortic regurgitation the symptoms provide a sharp contrast to the minimal symptoms of chronic, compensated aortic regurgitation; the left ventricle quickly exhausts its preload reserve (ability to dilate in response to the volume load) and, in the absence of hypertrophy, a sudden elevation in end-diastolic pressure leads to symptoms of pulmonary venous congestion (dyspnea) and sympathetic discharge (tachycardia and diaphoresis). The progression of symptoms to pronounced dyspnea at rest may take only a few days, or it may occur over several weeks or months.

The causes of acute aortic regurgitation include bacterial endocarditis, aortic dissection, ruptured aortic cusp (due to Marfan syndrome or myxomatous valve degeneration), trauma or sinus of Valsalva aneurysm. Chronic aortic regurgitation can be due to any of these, as well as to rheumatic heart disease, congenital malformations, syphilis, certain rheumatic diseases (ankylosing spondylitis), hypertensive dilatation of the aortic root and aortitis. Therefore, in evaluating a case of aortic regurgitation, the physician must pay appropriate attention to the historical and physical clues to the many possible underlying causes.

The systemic blood pressure in aortic regurgitation is determined to a large extent by the state of the peripheral vessels; consequently, the pulse pressure (systolic-diastolic) in aortic regurgitation may vary widely as a function of peripheral vascular resistance and heart rate. In determining the diastolic pressure, care must be taken to note the point at which the Korotkoff sounds become muffled—pistol shot sounds may continue down to zero, but the true diastolic pressure is rarely less than 40 mm of mercury. Hill sign, a pulse pressure measured in the leg which exceeds that in the arm by 40 mm of mercury, is generally accepted to imply severe aortic regurgitation (despite lack of careful hemodynamic substantiation). The increased stroke volume accompanying significant aortic regurgitation produces a carotid pulse with a rapid upstroke and diastolic collapse which may be bisferiens, as well as other signs accompanying a wide pulse pressure which include pistol shot sounds over peripheral arteries, Duroziez's to-and-fro bruit (produced by light stethoscope pressure over the femoral artery) and visible capillary pulsations in the nail beds.

The cardiac apical impulse is almost always displaced, enlarged and sustained in chronic severe regurgitation. The high pitched diastolic decrescendo murmur of aortic regurgitation is heard best at the aortic area or apex with the patient upright and the breath held in expiration. Aortic regurgitation due to aortic root dilatation is often louder on the right of the sternum in the fourth intercostal space, while that due to valvular disease is best heard on the left side. Cooing or musical diastolic murmurs suggest eversion of an aortic cusp vibrating in the regurgitant stream. In chronic aortic regurgitation, moderate severity is usually accompanied by a nearly holodiastolic murmur; however, exceptions are frequent enough to make this sign unreliable. The systolic flow murmur present with moderate or severe aortic regurgitation is short and occurs early in systole.

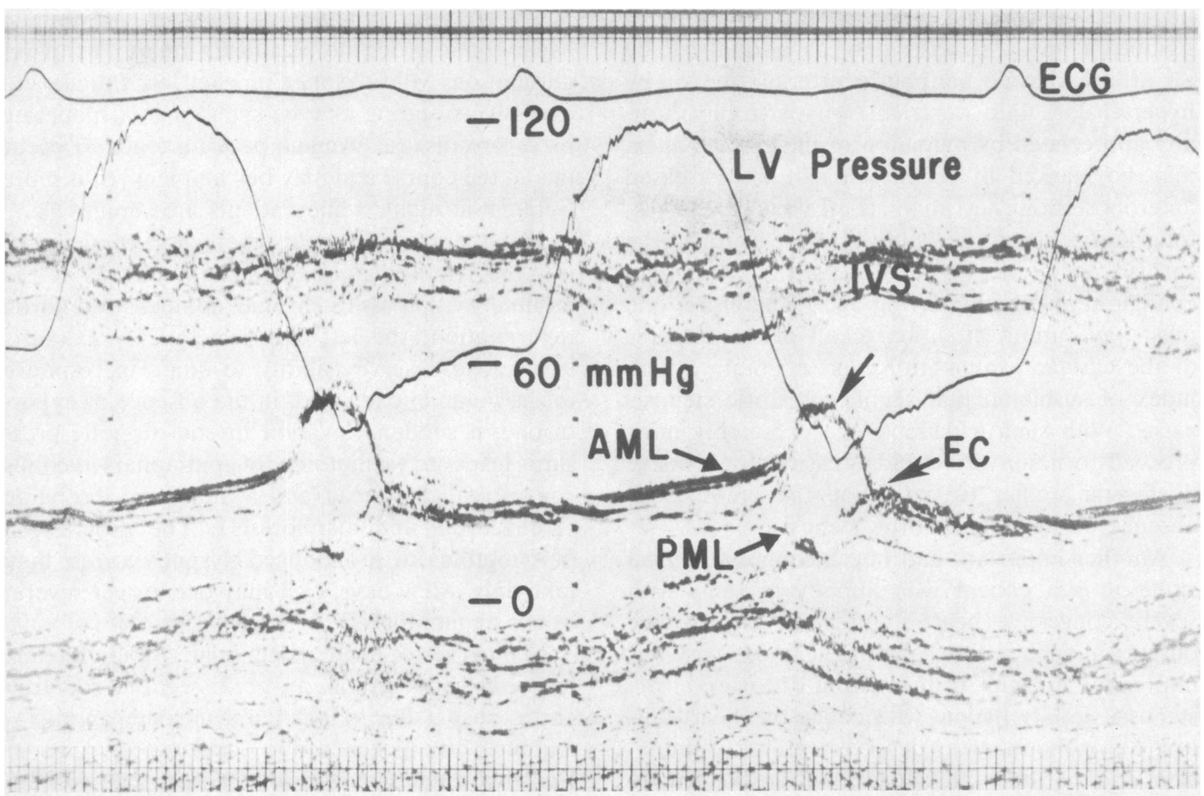


**Figure 5.**—Echocardiogram of the mitral valve and simultaneous left ventricular pressure in a patient with acute aortic insufficiency due to endocarditis. AML=anterior mitral leaflet; PML=posterior mitral leaflet; IVS=interventricular septum. Diastolic fluttering of the AML is present **(unlabeled arrow).** Early closure (EC) of the mitral valve is apparent with notably elevated left ventricular diastolic pressure; aortic regurgitation continues but filling across the mitral valve occurs only early in diastole.

Longer, late peaking systolic murmurs suggest concomitant aortic stenosis. The Austin Flint murmur is a low frequency diastolic rumble, often with presystolic accentuation, heard at the left ventricular apex with the patient in the left lateral decubitus position using light pressure on the bell of the stethoscope. This murmur is presumably generated by the anterior mitral leaflet being "pushed" toward its closed position into the path of antegrade mitral flow by the aortic regurgitant stream; earlier onset and longer Austin-Flint rumbles correlate with more severe aortic regurgitation.[30,31] Differentiation of this murmur from anatomic mitral stenosis is important; a true mitral stenosis rumble will increase after inhalation of amyl nitrite or exercise, due to increased mitral flow, whereas the Austin Flint rumble will diminish after amyl nitrite inhalation as aortic regurgitation becomes less. An $S_3$ or ventricular diastolic gallop is usually present in moderate aortic regurgitation; its presence does not imply left ventricular failure. An $S_4$ gallop in younger patients is an important clinical sign and suggests latent left ventricular dysfunction.

An important problem in chronic aortic regurgitation is the recognition of associated hypertensive disease. Clues to significant hypertension include diastolic blood pressures greater than 80 mm of mercury, systolic pressures greater than 160 mm of mercury and left ventricular hypertrophy out of proportion to the severity of aortic regurgitation. Since diastolic hypertension increases the volume of regurgitation, its treatment takes on special importance.

The physical signs in acute aortic regurgitation, in contrast to those in chronic aortic regurgitation, are characterized by the early onset of congestive heart failure, pulmonary edema and right ventricular failure. The pulse pressure may not be notably wide and the diastolic murmur may be short and soft, at least in part due to the pronounced elevation in left ventricular diastolic pressure. This may lead to early closure of the mitral valve (Figure 5), with an associated sound in mid-diastole, and a soft or absent $S_1$ regardless of the PR interval.[32] Tachycardia and an $S_3$ gallop are almost always present. Severe congestive heart failure can develop with great rapidity in acute aortic regurgitation and carries a very poor prognosis without surgical intervention.

DR. JOHNSON: *Not uncommonly in patients with aortic valve disease, the history and physical examination leave significant questions about the severity of the underlying hemodynamic derangements. Dr. Martin LeWinter will discuss the value and use of various noninvasive diagnostic methods available to help solve these problems.*

# Use of Noninvasive Diagnostic Methods in Aortic Valve Disease

MARTIN LeWINTER, MD*

HELPFUL INFORMATION regarding diagnosis and management of patients with aortic valve disease can be gained from the use of various noninvasive methods, particularly systolic time intervals and echocardiography.

*Systolic Time Intervals*

Because valvular aortic stenosis so directly and distinctively affects the systemic arterial pulse, the use of indices derived from the indirect recording of the arterial pulse is one of the most helpful noninvasive laboratory studies that can be done in evaluating an aortic outflow murmur. Indirect pulse wave recording from the carotid artery in the neck is a technically simple and reproducible method for calculation of these indices. The carotid pulse, electrocardiogram and phonocardiogram are recorded (Figure 4) at rapid paper speed and ten cardiac cycles are averaged at mid-expiration. The onset of the carotid upstroke is obtained by visual inspection, and the end of ejection is taken at the trough of the dicrotic notch. Several indices derived from these measurements correlate with significant valvular aortic stenosis; among these are the maximum rate of rise of arterial pulse (lower limit of normal 500 mm of mercury per second),[33] the left ventricular ejection time (LVET), the carotid upstroke time and the Q-peak murmur time. The LVET corrected for heart rate and sex using appropriate regression equations (LVET index) has been shown to be both a sensitive and specific test for the detection of significant aortic stenosis; these studies indicate that if the LVET index exceeds 420 msec, significant aortic stenosis (a gradient of more than

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